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(54) Title of the Invention: A Topical Skin Agent

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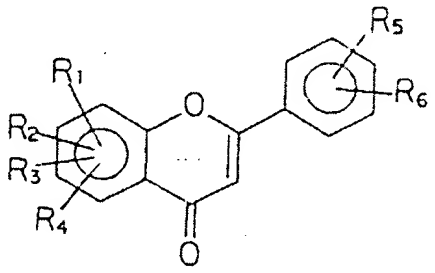
SPECIFICATION

Title of the Invention

A Topical Skin Agent

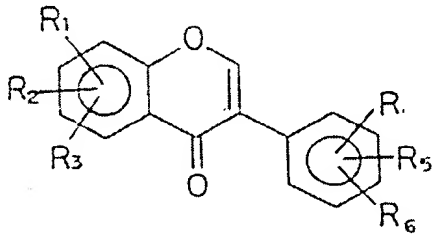
2. Claim

A topical skin agent characterized in that one or two or more flavone glycosides and/or isoflavone glycosides as indicated by general formulas (1) and (2) below are compounded.



General Formula (1)

(Wherein, R_1 is H, OH or OCH_3; R_2 is H, OH or OCH_3; R_3 is H, OH or OCH_3; R_4 is glucose, R_5 is OH or OCH_3; R_6 is OH or OCH_3.)



General Formula (2)

(Wherein, $R_1 = R_2 = OCH_2O$, R_3 is H or OH, R_4 is H or OH, R_5 is O-glucose or O-glucose-glucose, R_6 is H or R_1 is H, OH or OCH_3, R_2 is H, OH or OCH_3, R_3 is O-glucose, R_4 is H, OH or OCH_3, R_5 is H, OH or OCH_3, R_6 is H, OH or OCH_3.)

3. Detailed Description of the Invention

[Field of Industrial Use]

This invention relates to a topical skin agent that in addition to the effects of healing wounds and preventing and improving roughness of the skin also has the effects of preventing sagging of the skin and loss of luster and of stopping aging by compounding one or two or more flavone glycosides and/or isoflavone glycosides.

[Prior Art]

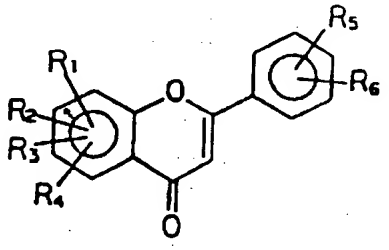
Allantoin, placenta extract, juvenile bovine serum sorukoseria [phonetic]*, aloe extract, black root [Symphytum officinale] extract and lithospermum root extract are compounded in topical skin agents for the purpose of healing wounds and preventing granulation and skin roughness. Allantoin produces glyoxilic acid and urea, which are highly irritating, in weal alkalis, placental extract and juvenile bovine serum sorukoseria [phonetic], which are proteins, and give off an unpleasant odor at high titers and aloe extract, black root and lithospermum root, which are natural substances, tend to produce turbidity, color change and odor change as well as presenting problems of safety. Moreover, their effectiveness is not satisfactory.

[Means for Solving the Problems]

The inventors, in the light of these circumstances, carried out intensive and repeated research. As a result, they perfected this invention by discovering a topical skin agent in which one or two or more flavone glycosides and/or isoflavone glycosides are compounded and are of superior effectiveness in healing wounds, preventing and improving roughness of the skin and stopping aging.

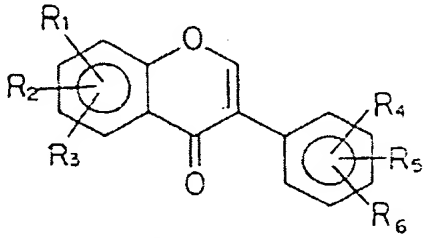
[Means for Solving the Problem]

Specifically, this invention is a topical skin agent characterized in that one or two or more flavone glycosides and/or isoflavone glycosides as indicated by general formulas (1) and (2) below are compounded.



General Formula (1)

(Wherein, R_1 is H, OH or OCH_3; R_2 isH, OH or OCH_3; R_3 is H, OH or OCH_3; R_4 is glucose, R_5 is OH or OCH_3; R_6 is OH or OCH_3.)



General Formula (2)

(Wherein, $R_1 = R_2 = OCH_2O$, R_3 is H or OH, R_4 is H or OH, R_5 is O-glucose or O-glucose-glucose [sic], R_6 is H or R_1 is H, OH or OCH_3, R_2 is H, OH or OCH_3, R_3 is O-glucose, R_4 is H, OH or OCH_3, R_5 is H, OH or OCH_3, R_6 is H, OH or OCH_3.)

The flavone glycosides and/or isoflavone glycosides of this invention may be both synthetic products or natural extracts. When they are natural products, they can be obtained by the methods described below.

Plants such as Iris florentina L. of the family Iridaceae, genus Iris, are heated and subjected to reflux or immersed in one or two or more solvents, for example, esters such as ethyl acetate, butyl acetate and amyl acetate, ketones such as acetone, methyl ethyl ketone and acetyl acetone and alcohols such as methanol, ethanol and butanol. The material that is obtained is then filtered and the extract that is obtained can be concentrated and purified. At this time, extraction may be performed in advance with a nonpolar solvent such as hexane in order to remove hydrophobic components. The extracts that are obtained by this method can be further subjected to silica gel column chromatography, eluted with a mixed solvent such as chloroform-methanol-water and fractionated, with a crude product being obtained. This product can be further subjected to reverse phase chromatography such as $C_{18[?]}$ and various flavone glycosides and isoflavone glycosides can be obtained.

The quantity of flavone glycoside and/or isoflavone glycoside compounded in this invention should be 0.000001 to 5%, and, preferably, 0.00005 to 1% as dry matter relative to the total volume of the topical skin agent. When it is less than 0.000001%, the effect of this invention is not sufficiently manifested. This is not desirable.

In addition to the essential components described above, as required, various components that are commonly used in cosmetic products, topical medicinal drug products and medicinal drug products can be compounded with the topical skin agents of this invention. They can include, for example, powdered components such as titanium dioxide, mica and talc, oils such as avocado oil, macadamia nut oil, corn oil, olive oil, rapseseed oil, evening primrose oil, castor oil, sunflower oil, tea kernel oil[?, literal translation], rice bran oil, hohoba [phonetic] oil, cacao oil, coconut oil, squalene, squalane, tallow, vegetable wax, beeswax, candelilla wax, carnauba wax, whale tallow, lanolin, liquid paraffin, sericine, vaseline, polyoxyethylene (8 mol) oleyl alcohol ether and glycerolmonooleate, higher

*Translator's Note: Transliterated phonetically from the Japanese. As such, the spelling may differ from other transliterations.

alcohols such as capryl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol, cholesterol and phytosterols, higher fatty acids such as caprylic acid, lauric acid, myristic acid, palmitic acid, stearic acid, behenic acid, lanolin fatty acid, linolic acid and linoleic acid, ultraviolet ray absorbents such as p-aminobenzoic acid, homomenthyl-7N-acetyl anthranilate, butyl methoxydibenzoyl methane, di-p-methoxysilicic acid-mono-2-ethylhexanoic acid glycerol, amyl salicylate, octyl cinnamate and 2,4-dihydroxybenzophenone, humectants such as polyethylene glycol, glycerol, sorbitol, xylitol, maltitol, mucopolysaccharides, hyaluronic acid, chondriotin sulfuric acid, chitosan and carboxymethyl chitin (salt), thickeners such as methyl cellulose, ethyl cellulose, carboxymethyl cellulose, gum arabic, polyvinyl alcohol, montmorillonite and saponite, organic solvents such as ethanol and 1,3-butyieneglycol, antioxidants such as butyl hydroxytoluene, tocopherol and phytic acid, antibacterial preservatives such as benzoic acid, salicylic acid, sorbitan acids, dehydroacetic acid, p-oxybenzoic acid alkyl esters (ethylparaben, butylparaben,, etc.) and hexachlorophene, amino acids such as glycine, alanine, valine, leucine, serine, threonine, phenylalanine, tyrosine, aspartic acid, glutamic acid, asparagine, glutamine, taurine, arginine and histidine and alkali metal salts and hydrochlorides thereof, acyl sarcosine salts (for example, lauroyl sarcosinate), glutathione, organic acids such as citric acid, malic acid, tartaric acid and lactic acid, vitamins such as vitamin A and derivatives thereof, B vitamins such as vitamin B_6 hydrochloride, vitamin B_6 tripalmitate, vitamin B_6 dioctanoate, vitamin B_2 and derivatives thereof, vitamin B_{12} and vitamin B_{15} and derivatives thereof, C vitamins such as ascorbic acid, ascorbic acid sulfuric acid esters, ascorbic acid phosphoric acid esters and ascorbic acid dipalmitate, E vitamins such as α-tocopherol, β-tocopherol, γ-tocopherol, vitamin E acetate and vitamon E nicotinate, D vitamins, vitamin H, pantothenic acid and pantothene, various drugs such as nicotinic acid amide, benzyl nicotinamide, γ-oryzanol, allantoin, glycyrrrhizinic acid (salts), glycyrrhetinic acid and derivatives thereof, hinokitiol, mucicin, bisabolol, eucalyptol, phytosterol, thymol, inosotol, saponin, (saiko[phonetic = probably a plant] saponin, carrot saponin, luffa saponin, ,amuroji [phonetic = probably a plant] saponin, etc.), pantothenyl ethyl ether, ethynyl estradiol, cepharanthine and placenta extract, natural extracts obtained by extraction using organic solvents, alcohols, polyvalent alcohols, water and aqueous alcohols of licorice, paprika, Rabdosia japonica, Rabdosia trichocarpa, scabwort, rouge plant [literal translation, corresponding to existing English name], sorrel, Sophora flavescens, camphor tree, nuphar, Houtuynia cordata, haikazura [phonetic], celery, geranium, turmeric, dead nettle, oranges, sage, Western ivy, nagiikada [phonetic], yarrow, mistletoe, mallow, senkyu [phonetic], Japanese green gentian, thyme, cloves, dried orange peel, Angelica acutiloba var. acutiloba, marigold, Japanese spruce, carrot, garlic, wild rose, birch, parsley, gentiana, mint, fennel, field horsetail, saffron, watercress, soapwort, butcher's-broom, grapes, ivy, luffa, nettle, lime, hops, Japanese pepper, *shiitake* [Cortinellus shiitake], horse chestnut, buckbean, soapberry, melissa, peach, eucalyptus, gamboge, lithospermum root, strawberry geranium, arnica, lily, mugwort, beefsteak plant, peony, rosemary, lemon, shokyo [phonetic], eijitsu [phonetic], burnet, white birch, raspberry, ogon [phonetic], aloe, cucumber, burdock, gardenia, obaku [phonetic], goldthread, catechu, hydrangea, taiso [phonetic], Retinispora plumosa, *sawara* cypress, cayeene, Poria cocos, shelf fungus, umbellate pore fungus [*Polyporus umbellata*], *Fomes japonicus* and koso, pigments, nonionic surfactants such as sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan sesquioleate, sorbitan trioleate, polyoxyerthylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyethylene glycol monooleate, polyoxyethylene alkyl ethers, polyglycol diesters, lauryl diethanolamide and fatty acid isopropanolamides, cationic surfactants such as stearyl trimethylammonium chloride and benzalkonium choride, anionic surfactants such as sodium palmitate, sodium laurate, sodium lauryl sulfate, potassium lauryl sulfate, alkyl sulfuric acid triethanolamine ether, Turkey red oil, linear dodecyl benzene sulfate and polyoxyethylene hardened castor oil maleic acid, amphoteric surfactants, fragrances and purified water. The preparation of the topical skin agent of this invention can be in any desired form. For example, the forms that they can take include solubilized systems and emulsions for toilet water, emulsified systems for creams, dispersed solutions for foundations or ointments.

Next, we shall present examples of the manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside and isoflavone-7-O-β-D-glucoside.

(Example of Manufacture 1) Example of manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside

1.5 kg of roots and stems of Iris florentina L. were extracted with 40% water-containing ethanol and the product was concentrated. This product was suspended in water and was distributed successively in chloroform, ethyl acetate and n-butanol. The n-butanol layer was concentrated, after which extraction was performed with a mixed solvent comprised of chloroform, methanol and water. The extraction component in which the mixture ratio was 6 : 4 : 0 - 6 : 4 : 0.5 were concentrated. It was further subjected to $C_{18[?]}$ reverse phase chromatography by high-pressure liquid chromatography, extraction was performed with 53% water-containing methanol and 100 mg of Example of manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside was obtained.

(Example of Manufacture 2) Example of manufacture of isoflavone-7-O-β-D-glucoside

A 10 ml acetone solution of 1 g of 2,4-dioxyphenylbenzyl ketone, 1 g of benzyl chloride and 1.2 g of anhydrous potassium carbonate was boiled and reacted for 8 hours over a water bath. The reactants were poured into water and were allowed to stand for 12 hours, after which the precipitate was collected and recrystallized with ethanol, with 0.5 g of crystals of benzyl ether being obtained. A solution comprised of 6.3 g of benzyl ether dissolved in 150 ml of ethyl formate was slowly added dropwise onto 4 g of sodium cooled with salt*. After 12 hours, the paste-like mass was poured onto ice, the ethyl formate was distilled off and the aqueous solution was extracted with ether. The extract solution was washed with an aqueous solution of sodium hydroxide cooled with ice and washed again with water. It was desiccated with magnesium sulfate and the ether distilled off. When ethanol was added to the remaining oleaginous substance, it underwent recrystallization. Recrystallization was effected with ethanol, glacial acetic acid and ethyl acetate and 3.0 g of colorless crystals of 7-benzyloxyisoflavone was obtained. This product was boiled with concentrated hydrochloric acid in glacial acetic acid, the benzyl groups were removed and 2.5 g of 7-hydroxyisoflavone was obtained.

Next, 1 g of 2,3,4,6-tetra-O-acetyl-α-D-bromohexose was dissolved in 10 ml of chloroform, 5 ml of aqueous solution of 1.25 N sodium hydroxide in which 1 g of 7-hydroxyisoflavone and benzyl triethylammonium bromide were dissolved was added as the materials were being stirred and heating and refluxing were performed for 3 hours at 60°C. Following this, 100 ml of water and 100 ml of chloroform were added, distribution was effected and the chloroform layer was washed with an aqueous solution of 1.25 N sodium hydroxide. The chloroform layer was concentrated, after which recrystallization was effected with ethanol and 1.9 g of isoflavone-7-O-β-D-tetraacetyl glucoside was obtained. This product was boiled with dilute sulfuric acid and 1.0 g of isoflavone-7-O-β-D-glucoside was obtained.

The flavone glycoside and the isoflavone glycoside obtained by this invention were odorless even when compounded with topical skin agents and did not produce any precipitates or turbidity.

[Effect of the Invention and Examples of Formulation]

The following tests of skin cell growth promoting action were performed in order to show the effects of flavone glycosides and isoflavone glycosides in wound healing, preventing and improving rough skin and of their effects in preventing sagging of skin, loss of luster and aging.

(Skin cell growth promoting action)

Human skin tissue was cut into fine strips which were attached to the bottom face of a laboratory dish for cell culture. When they were cultured for 1 week in Eagle's MEM culture medium (containing 10% bovine fetal serum), almost the entire bottom face of the laboratory dish was covered with tissue blastocytes. Single cells were isolated by treating these tissue blastocytes with a 0.25% trypsin solution. Next, a cell suspension of 10000 cells/ml was made, 0.1 ml of this solution was added per laboratory dish, Eagle's MEM culture medium and various types of flavone glycosides and isoflavone glycosides (final concentrations, 1 μg/ml) were added and culturing was performed for two weeks in a CO_2 incubator. Following that, the cells were immobilized and stained, after which the cell colonies were measured. Cases in which flavone glycosides and isoflavone glycosides were not added were used as the controls. Cell growth promotion rate was calculated by the following equation.

cell growth promotion rate (%) =

$$\frac{\text{number of colonies of cells treated by glycosides as described above}}{\text{number of colonies of control cells}} \times 100$$

Table 1 shows the cell growth promotion rates after two weeks of culturing. The evaluation method is indicated below.

* Translator's Note: Probably a misprint in the Japanese

Evaluation

◎ cell growth promotion rate 150% or greater
○ cell growth promotion rate 100 % to 150%
x cell growth promotion rate less than 100%

Table 1. Cell growth promotion rate

Drug	Evaluation
Iris florentina L. extract	○
5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside	◎
5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside	◎
isoflavone-7-β-D-glycoside	◎

It was found that such flavone glycosides and isoflavone glycosides as 5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside, 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside and isoflavone-7-β-D-glycoside had particularly strong cell growth promotion action.

(Working Test)

The effect on rough skin based on a working test is shown below.

-- Test Method --

The study was conducted using a total of 10 groups of healthy women complaining of rough skin, with 10 subjects per group. Lotion compounded of the formulation shown in Table 2 was applied to the face and roughness of the skin was evaluarted after 1 week, with an overall evaluation being made.

- Test Material-

Lotion compounded of the formulation shown in Table 2 was used as the test material.

The compounding quantities are in weight %. The compounding quantities of the flavone glycosides and isoflavone glycosides are for dried substances.

Table 2. Formulations of Lotion for Test Use

"Formulation

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) Iris florentina L. extract 0.1%
6) Purified water remainder

"Formulation 2

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) 5-Hydroxy-7-methoxy-4'-hydroxyflavone -6-O-β-D-glycoside 0.0001%
6) Purified water remainder

"Formulation 3"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) 5-Methoxy-6,7-methylenedioxy isoflavone -4'-O-β-D-glycoside 0.001%
6) Purified water remainder

'Formulation 4"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) isoflavone-7-β-D-glycoside 0.0002%
6) Purified water remainder

-- Evaluative criteria for roughness of skin --

Markedly effective	Rough skin was essentially not pronounced after 1 week.
Effective:	Rough skin was extremely slight after 1 week.
Moderately effective	Rough skin was fairly slight after 1 week.
Ineffective	There was no change in rough skin after 1 week.

-- Evaluations of rough skin --

◎: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was greater than 60%

O: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was 20% to 60%

X: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was less than 20%

Table 3. Effectiveness in Improvement of Skin Roughness

Comparison Case 1	Formulation Case 1	Formulation Case 2	Formulation Case 3	Formulation Case 4
x	O	◎	◎	◎

The same formulation was used in Comparison Case 1 in Table 3 as in Compartison Case 1 except that hot water extract of Iris florentina L. extract was excluded.

As should be evident from Table 3, it was found that formulations in which flavone glycosides and isoflavone glycosides such as 5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside, 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside, isoflavone-7-β-D-glycoside and Iris florentina L. hot water extract were compounded and had excellent effectiveness in improving skin roughness.

[Examples]

Next, we shall present a detailed description of this invention by means of examples. This invention is not limited by them. The quantities compounded are indicated as weight %. The compounding quantities of flavone glycoside and isoflavone glycoside are as dry substance.

Example 1, Toilet Water

(1) 5,4'-hydroxy-7-methoxyflavone-8-C-β-D-glycoside	1.0%
(2) Glycerol	4.0%
(3) 1,3-butylene glycol	4.0%
(4) Ethanol	7.0%
(5) Polyoxyethylene oleyl alcohol	0.5%
(6) Methylparaben	0.05%
(7) Citric acid	0.01%
(8) Sodium citrate	0.1%
(9) Fragrances	0.05%
(10) Purified water	remainder

(Preparation Method)

Citric acid, sodium citrate, glycerol and 1,3-butylene glycol were dissoved in purified water. Separately, polyoxyethylene oleyl alcohol, 5,4'-hydroxy-7-methoxyflavone-8-C-β-D-glycoside, fragrances and methylparaben were dissolved in ethanol. This solution was then added to the aforementioned purified water solution, solubilized and filtered, with toilet water being obtained.

Example 2, Cream

(1) Cetostearyl alcohol	3.5%
(2) Squalane	40.0%
(3) Beeswax	3.0%
(4) Reduced lanolin	5.0%
(5) Ethylparaben	0.3%
(6) Polyoxyethylene (20) sorbitan monopalmitic acid ester	2.0%
(7) Stearic acid monoglyceride	2.0%
(8) 5-hydroxy-7-methoxy-4'-hydroxyflavone -6-C-β-D-glucoside	0.000001%
(9) Fragrances	0.03%
(10) 1,3-butylene glycol	5.0%
(11) Glycerol	5.0%
(12) Sodium hyaluronate	0.05%
(13) Purified water	remainder

(Preparation Method)

A solution that was obtained by heating and dissolving (1), (2), (3), (4), (5), (6), (7), (8) and (9) and maintaining it at 75°C was added to (10), (11), (12) and (13) that had been heated to 75°C as the materials were being stirred. The mixture was treated in an homogenizer and the emulsified particles were finely pulverized, after which it was rapidly cooled, with a cream being obtained.

Example 3, Emulsion

(1) 5-methoxy-6,7-methylenedioxy isoflavone -4'-O-β-D-glucoside	0.001%
(2) Stearic acid	1.5%
(3) Cetyl alcohol	0.5%
(4) Beeswax	2.0%
(5) Polyoxyethylene (10) monooleic acid ester	1.0%
(6) Glycerol monostearic acid ester	1.0%
(7) Quince seed extract (5% aqueous solution)	20.0%

(8) Propylene glycol	5.0%
(9) Ethanol	3.0%
(10) Ethylparaben	0.3%
(11) Fragrances	0.03%
(12) Purified water	remainder

(Preparation Method)

The 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glucoside and fragrances were added to ethanol and dissolved (alcohol phase). Propylene glycol was added to purified water in which it was dissolved by heating and maintained at 70°C (aqueous phase). The other components except for the quince seed extract were mixed in, dissolved by heating and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and preliminary emulsification was performed, with uniform emulsification being effected with an homogenizer. The alcohol phase and the quince seed extract were added as the mixture was being stirred. Following that, the materials were cooled to 30°C, with an emulsion being obtained.

Example 4, Pack

(1) Isoflavone-7-O-β-D-glucoside	0.1%
(2) Polyvinyl alcohol	15.0%
(3) Polyethylene glycol	3.0%
(4) Propylene glycol	7.0%
(5) Ethanol	10.0%
(6) Methylparaben	0.05%
(7) Fragrances	0.05%
(8) Purified water	remainder

(Preparation Method)

Polyethylene glycol, propylene glycol and methylparaben were added to purified water and were dissolved by stirring. Next, the polyvinyl alcohol was added and was heated and stirred. An ethanol solution in which the isoflavone-7-O-β-D-glucoside and fragrances were dissolved was added and the mixture was dissolved by heating, with a pack being obtained.

Example 5, Cosmetic Material for Scalp Use

(1) 5-hydroxy-6,4'-methoxyisoflavone-7 -O-β-D-glucoside	2.0%
(2) 1,3-butylene glycol	6.5%
(3) Polyethylene glycol 1500	5.0%
(4) Ethanol	5.5%
(5) Potassium hydroxide	0.05%
(6) Purified water	45.45%
(7) 2-hexyldecylpalmitate	10.0%
(8) Squalane	5.0%
(9) Butylparaben	0.2%
(10) Vitamin C	0.15%
(11) Fragrances	0.05%
(12) Purified water	19.9%
(13) Carboxyvinyl polymer	0.2%

(Preparation Method)

A solution comprised of (7), (8), (9), (10) and (11) that had been dissolved at 75°C was added to (1), (2), (3), (4) and (6), which were being maintained at 75°C as the materials were being stirred. Further, (5), (12) and (13) were added at room temperature as they were being dissolved by stirring. The solution was then cooled while being stirred, with a scalp treatment being obtained.

Example 6, Ointment

(1) 5-methoxy-6,7-methylenedioxyisoflavone -4-O-β-D-glucoside	5.0%
(2) Stearyl alcohol	18.0%
(3) Vegetable wax	20.0%
(4) Polyoxyethylene (10) monooleic acid ester	0.25%
(5) Glycerol monostearic acid ester	0.25%
(6) Vaseline	40.0%
(7) Purified water	16.5%

(Preparation Method)

The purified water was maintained at 70°C (aqueous phase). The other constituents were mixed and dissolved at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and emulsification to a homogeneous state was effected with an homogenizer, after which the emulsion was cooled and an ointment was obtained.

Example 7, Toilet Water

(1) 5,4'-hydroxyflavone-8-O-β-D -glucoside	0.00003%
(2) 5-methoxy-6,7-methylenedioxyisoflavone--4'-O-β-D-glucoside	0.00002%
(3) Glycerol	4.0%
(4) 1,3-butylene glycol	4.0%
(5) Ethanol	7.0%
(6) Polyoxyethylene oleyl alcohol	0.5%
(7) Methylparaben	0.05%
(8) Citric acid	0.01%

(9) Sodium citrate	0.1%
(10) Fragrances	0.05%
(11) Purified water	remainder

(Preparation Method)

The citric acid, sodium citrate, glycerol and 1,3-butylene glycol were dissolved in the purified water. Separately, the 5,4'-hydroxyflavone-8-O-β-D-glucoside, 5-methoxy-6,7-methylenedioxyisoflavone-4'-O-β-D-glucoside, fragrances and methylparaben were dissolved in ethanol, this solution was added to the aforementioned purified water solution and the mixture was solubilized and filtered, with toilet water being obtained.

The cosmetic materials obtained in Examples 1 to 7 exhibited superior effectiveness in wound healing, preventing and improving skin roughness and in preventing aging in terms of sagging of the skin and loss of luster.

Applicant: Shiseido Company, Ltd.

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(54) Title of the Invention: A Topical Skin Agent

(21) Application No.: 62-255292

(22) Application Date: 9 October 1987

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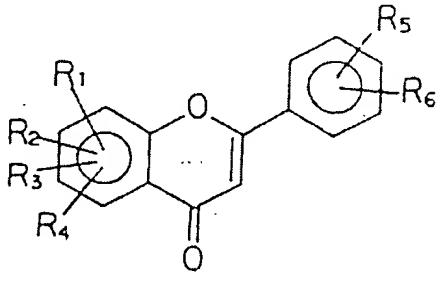
SPECIFICATION

1. Title of the Invention

A Topical Skin Agent

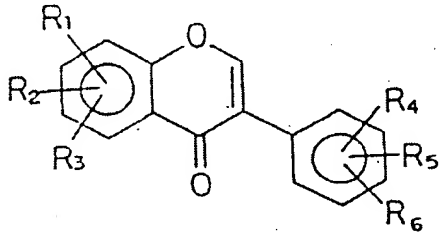
2. Claim

A topical skin agent characterized in that one or two or more flavone glycosides and/or isoflavone glycosides as indicated by general formulas (1) and (2) below are compounded.



General Formula (1)

(Wherein, R_1 is H, OH or OCH_3; R_2 is H, OH or OCH_3; R_3 is H, OH or OCH_3; R_4 is glucose, R_5 is OH or OCH_3; R_6 is OH or OCH_3.)



General Formula (2)

(Wherein, $R_1 = R_2 = OCH_2O$, R_3 is H or OH, R_4 is H or OH, R_5 is O-glucose or O-glucose-glucose, R_6 is H or R_1 is H, OH or OCH_3, R_2 is H, OH or OCH_3, R_3 is O-glucose, R_4 is H, OH or OCH_3, R_5 is H, OH or OCH_3, R_6 is H, OH or OCH_3.)

3. Detailed Description of the Invention

[Field of Industrial Use]

This invention relates to a topical skin agent that in addition to the effects of healing wounds and preventing and improving roughness of the skin also has the effects of preventing sagging of the skin and loss of luster and of stopping aging by compounding one or two or more flavone glycosides and/or isoflavone glycosides.

[Prior Art]

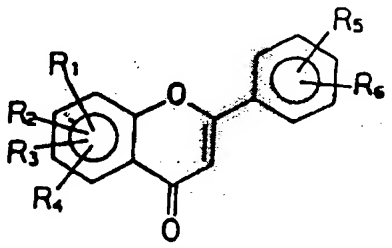
Allantoin, placenta extract, juvenile bovine serum sorukoseria [phonetic]*, aloe extract, black root [Symphytum officinale] extract and lithospermum root extract are compounded in topical skin agents for the purpose of healing wounds and preventing granulation and skin roughness. Allantoin produces glyoxilic acid and urea, which are highly irritating, in weal alkalis, placental extract and juvenile bovine serum sorukoseria [phonetic], which are proteins, and give off an unpleasant odor at high titers and aloe extract, black root and lithospermum root, which are natural substances, tend to produce turbidity, color change and odor change as well as presenting problems of safety. Moreover, their effectiveness is not satisfactory.

[Means for Solving the Problems]

The inventors, in the light of these circumstances, carried out intensive and repeated research. As a result, they perfected this invention by discovering a topical skin agent in which one or two or more flavone glycosides and/or isoflavone glycosides are compounded and are of superior effectiveness in healing wounds, preventing and improving roughness of the skin and stopping aging.

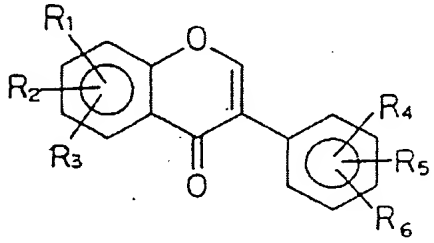
[Means for Solving the Problem]

Specifically, this invention is a topical skin agent characterized in that one or two or more flavone glycosides and/or isoflavone glycosides as indicated by general formulas (1) and (2) below are compounded.



General Formula (1)

(Wherein, R_1 is H, OH or OCH_3; R_2 isH, OH or OCH_3; R_3 is H, OH or OCH_3; R_4 is glucose, R_5 is OH or OCH_3; R_6 is OH or OCH_3.)



General Formula (2)

(Wherein, $R_1 = R_2 = OCH_2O$, R_3 is H or OH, R_4 is H or OH, R_5 is O-glucose or O-glucose-glucose [sic], R_6 is H or R_1 is H, OH or OCH_3, R_2 is H, OH or OCH_3, R_3 is O-glucose, R_4 is H, OH or OCH_3, R_5 is H, OH or OCH_3, R_6 is H, OH or OCH_3.)

The flavone glycosides and/or isoflavone glycosides of this invention may be both synthetic products or natural extracts. When they are natural products, they can be obtained by the methods described below.

Plants such as Iris florentina L. of the family Iridaceae, genus Iris, are heated and subjected to reflux or immersed in one or two or more solvents, for example, esters such as ethyl acetate, butyl acetate and amyl acetate, ketones such as acetone, methyl ethyl ketone and acetyl acetone and alcohols such as methanol, ethanol and butanol. The material that is obtained is then filtered and the extract that is obtained can be concentrated and purified. At this time, extraction may be performed in advance with a nonpolar solvent such as hexane in order to remove hydrophobic components. The extracts that are obtained by this method can be further subjected to silica gel column chromatography, eluted with a mixed solvent such as chloroform-methanol-water and fractionated, with a crude product being obtained. This product can be further subjected to reverse phase chromatography such as C_{18} and various flavone glycosides and isoflavone glycosides can be obtained.

The quantity of flavone glycoside and/or isoflavone glycoside compounded in this invention should be 0.000001 to 5%, and, preferably, 0.00005 to 1% as dry matter relative to the total volume of the topical skin agent. When it is less than 0.000001%, the effect of this invention is not sufficiently manifested. This is not desirable.

In addition to the essential components described above, as required, various components that are commonly used in cosmetic products, topical medicinal drug products and medicinal drug products can be compounded with the topical skin agents of this invention. They can include, for example, powdered components such as titanium dioxide, mica and talc, oils such as avocado oil, macadamia nut oil, corn oil, olive oil, rapseseed oil, evening primrose oil, castor oil, sunflower oil, tea kernel oil[?, literal translation], rice bran oil, hohoba [phonetic] oil, cacao oil, coconut oil, squalene, squalane, tallow, vegetable wax, beeswax, candelilla wax, carnauba wax, whale tallow, lanolin, liquid paraffin, sericine, vaseline, polyoxyethylene (8 mol) oleyl alcohol ether and glycerolmonooleate, higher

*Translator's Note: Transliterated phonetically from the Japanese. As such, the spelling may differ from other transliterations.

alcohols such as capryl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol, cholesterol and phytosterols, higher fatty acids such as caprylic acid, lauric acid, myristic acid, palmitic acid, stearic acid, behenic acid, lanolin fatty acid, linolic acid and linoleic acid, ultraviolet ray absorbents such as p-aminobenzoic acid, homomenthyl-7N-acetyl anthranilate, butyl methoxydibenzoyl methane, di-p-methoxysilicic acid-mono-2-ethylhexanoic acid glycerol, amyl salicylate, octyl cinnamate and 2,4-dihydroxybenzophenone, humectants such as polyethylene glycol, glycerol, sorbitol, xylitol, maltitol, mucopolysaccharides, hyaluronic acid, chondriotin sulfuric acid, chitosan and carboxymethyl chitin (salt), thickeners such as methyl cellulose, ethyl cellulose, carboxymethyl cellulose, gum arabic, polyvinyl alcohol, montmorillonite and saponite, organic solvents such as ethanol and 1,3-butyleneglycol, antioxidants such as butyl hydroxytoluene, tocopherol and phytic acid, antibacterial preservatives such as benzoic acid, salicylic acid, sorbitan acids, dehydroacetic acid, p-oxybenzoic acid alkyl esters (ethylparaben, butylparaben,, etc.) and hexachlorophene, amino acids such as glycine, alanine, valine, leucine, serine, threonine, phenylalanine, tyrosine, aspartic acid, glutamic acid, asparagine, glutamine, taurine, arginine and histidine and alkali metal salts and hydrochlorides thereof, acyl sarcosine salts (for example, lauroyl sarcosinate), glutathione, organic acids such as citric acid, malic acid, tartaric acid and lactic acid, vitamins such as vitamin A and derivatives thereof, B vitamins such as vitamin B_6 hydrochloride, vitamin B_6 tripalmitate, vitamin B_6 dioctanoate, vitamin B_2 and derivatives thereof, vitamin B_{12} and vitamin B_{15} and derivatives thereof, C vitamins such as ascorbic acid, ascorbic acid sulfuric acid esters, ascorbic acid phosphoric acid esters and ascorbic acid dipalmitate, E vitamins such as α-tocopherol, β-tocopherol, γ-tocopherol, vitamin E acetate and vitamon E nicotinate, D vitamins, vitamin H, pantothenic acid and pantothene, various drugs such as nicotinic acid amide, benzyl nicotinamide, γ-oryzanol, allantoin, glycyrrrhizinic acid (salts), glycyrrhetinic acid and derivatives thereof, hinokitiol, mucicin, bisabolol, eucalyptol, phytosterol, thymol, inosotol, saponin, (saiko[phonetic = probably a plant] saponin, carrot saponin, luffa saponin, ,amuroji [phonetic = probably a plant] saponin, etc.), pantothenyl ethyl ether, ethynyl estradiol, cepharanthine and placenta extract, natural extracts obtained by extraction using organic solvents, alcohols, polyvalent alcohols, water and aqueous alcohols of licorice, paprika, Rabdosia japonica, Rabdosia trichocarpa, scabwort, rouge plant [literal translation, corresponding to existing English name], sorrel, Sophora flavescens, camphor tree, nuphar, Houtuynia cordata, haikazura [phonetic], celery, geranium, turmeric, dead nettle, oranges, sage, Western ivy, nagiikada [phonetic], yarrow, mistletoe, mallow, senkyu [phonetic], Japanese green gentian, thyme, cloves, dried orange peel, Angelica acutiloba var. acutiloba, marigold, Japanese spruce, carrot, garlic, wild rose, birch, parsley, gentiana, mint, fennel, field horsetail, saffron, watercress, soapwort, butcher's-broom, grapes, ivy, luffa, nettle, lime, hops, Japanese pepper, *shiitake* [Cortinellus shiitake], horse chestnut, buckbean, soapberry, melissa, peach, eucalyptus, gamboge, lithospermum root, strawberry geranium, arnica, lily, mugwort, beefsteak plant, peony, rosemary, lemon, shokyo [phonetic], eijitsu [phonetic], burnet, white birch, raspberry, ogon [phonetic], aloe, cucumber, burdock, gardenia, obaku [phonetic], goldthread, catechu, hydrangea, taiso [phonetic], Retinispora plumosa, *sawara* cypress, cayeene, Poria cocos, shelf fungus, umbellate pore fungus [*Polyporus umbellata*], *Fomes japonicus* and koso, pigments, nonionic surfactants such as sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan sesquioleate, sorbitan trioleate, polyoxyerthylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyethylene glycol monooleate, polyoxyethylene alkyl ethers, polyglycol diesters, lauryl diethanolamide and fatty acid isopropanolamides, cationic surfactants such as stearyl trimethylammonium chloride and benzalkonium choride, anionic surfactants such as sodium palmitate, sodium laurate, sodium lauryl sulfate, potassium lauryl sulfate, alkyl sulfuric acid triethanolamine ether, Turkey red oil, linear dodecyl benzene sulfate and polyoxyethylene hardened castor oil maleic acid, amphoteric surfactants, fragrances and purified water. The preparation of the topical skin agent of this invention can be in any desired form. For example, the forms that they can take include solubilized systems and emulsions for toilet water, emulsified systems for creams, dispersed solutions for foundations or ointments.

Next, we shall present examples of the manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside and isoflavone-7-O-β-D-glucoside.

(Example of Manufacture 1) Example of manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside

1.5 kg of roots and stems of Iris florentina L. were extracted with 40% water-containing ethanol and the product was concentrated. This product was suspended in water and was distributed successively in chloroform, ethyl acetate and n-butanol. The n-butanol layer was concentrated, after which extraction was performed with a mixed solvent comprised of chloroform, methanol and water. The extraction component in which the mixture ratio was 6 : 4 : 0 - 6 : 4 : 0.5 were concentrated. It was further subjected to $C_{18[?]}$ reverse phase chromatography by high-pressure liquid chromatography, extraction was performed with 53% water-containing methanol and 100 mg of Example of manufacture of 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β--D-glucoside was obtained.

(Example of Manufacture 2) Example of manufacture of isoflavone-7-O-β-D-glucoside

A 10 ml acetone solution of 1 g of 2,4-dioxyphenylbenzyl ketone, 1 g of benzyl chloride and 1.2 g of anhydrous potassium carbonate was boiled and reacted for 8 hours over a water bath. The reactants were poured into water and were allowed to stand for 12 hours, after which the precipitate was collected and recrystallized with ethanol, with 0.5 g of crystals of benzyl ether being obtained. A solution comprised of 6.3 g of benzyl ether dissolved in 150 ml of ethyl formate was slowly added dropwise onto 4 g of sodium cooled with salt*. After 12 hours, the paste-like mass was poured onto ice, the ethyl formate was distilled off and the aqueous solution was extracted with ether. The extract solution was washed with an aqueous solution of sodium hydroxide cooled with ice and washed again with water. It was desiccated with magnesium sulfate and the ether distilled off. When ethanol was added to the remaining oleaginous substance, it underwent recrystallization. Recrystallization was effected with ethanol, glacial acetic acid and ethyl acetate and 3.0 g of colorless crystals of 7-benzyloxyisoflavone was obtained. This product was boiled with concentrated hydrochloric acid in glacial acetic acid, the benzyl groups were removed and 2.5 g of 7-hydroxyisoflavone was obtained.

Next, 1 g of 2,3,4,6-tetra-O-acetyl-α-D-bromohexose was dissolved in 10 ml of chloroform, 5 ml of aqueous solution of 1.25 N sodium hydroxide in which 1 g of 7-hydroxyisoflavone and benzyl triethylammonium bromide were dissolved was added as the materials were being stirred and heating and refluxing were performed for 3 hours at 60°C. Following this, 100 ml of water and 100 ml of chloroform were added, distribution was effected and the chloroform layer was washed with an aqueous solution of 1.25 N sodium hydroxide. The chloroform layer was concentrated, after which recrystallization was effected with ethanol and 1.9 g of isoflavone-7-O-β-D-tetraacetyl glucoside was obtained. This product was boiled with dilute sulfuric acid and 1.0 g of isoflavone-7-O-β-D-glucoside was obtained.

The flavone glycoside and the isoflavone glycoside obtained by this invention were odorless even when compounded with topical skin agents and did not produce any precipitates or turbidity.

[Effect of the Invention and Examples of Formulation]

The following tests of skin cell growth promoting action were performed in order to show the effects of flavone glycosides and isoflavone glycosides in wound healing, preventing and improving rough skin and of their effects in preventing sagging of skin, loss of luster and aging.

(Skin cell growth promoting action)

Human skin tissue was cut into fine strips which were attached to the bottom face of a laboratory dish for cell culture. When they were cultured for 1 week in Eagle's MEM culture medium (containing 10% bovine fetal serum), almost the entire bottom face of the laboratory dish was covered with tissue blastocytes. Single cells were isolated by treating these tissue blastocytes with a 0.25% trypsin solution. Next, a cell suspension of 10000 cells/ml was made, 0.1 ml of this solution was added per laboratory dish, Eagle's MEM culture medium and various types of flavone glycosides and isoflavone glycosides (final concentrations, 1 μg/ml) were added and culturing was performed for two weeks in a CO_2 incubator. Following that, the cells were immobilized and stained, after which the cell colonies were measured. Cases in which flavone glycosides and isoflavone glycosides were not added were used as the controls. Cell growth promotion rate was calculated by the following equation.

cell growth promotion rate (%) =

$$\frac{\text{number of colonies of cells treated by glycosides as described above}}{\text{number of colonies of control cells}} \times 100$$

Table 1 shows the cell growth promotion rates after two weeks of culturing. The evaluation method is indicated below.

* Translator's Note: Probably a misprint in the Japanese

Evaluation

◎: cell growth promotion rate 150% or greater
○: cell growth promotion rate 100 % to 150%
x : cell growth promotion rate less than 100%

Table 1. Cell growth promotion rate

Drug	Evaluation
Iris florentina L. extract	○
5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside	◎
5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside	◎
isoflavone-7-β-D-glycoside	◎

It was found that such flavone glycosides and isoflavone glycosides as 5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside, 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside and isoflavone-7-β-D-glycoside had particularly strong cell growth promotion action.

(Working Test)

The effect on rough skin based on a working test is shown below.

Test Method --

The study was conducted using a total of 10 groups of healthy women complaining of rough skin, with 10 subjects per group. Lotion compounded of the formulation shown in Table 2 was applied to the face and roughness of the skin was evaluarted after 1 week, with an overall evaluation being made.

Test Material-

Lotion compounded of the formulation shown in Table 2 was used as the test material.

The compounding quantities are in weight %. The compounding quantities of the flavone glycosides and isoflavone glycosides are for dried substances.

Table 2. Formulations of Lotion for Test Use

"Formulation 1"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) Iris florentina L. extract 0.1%
6) Purified water remainder

"Formulation 2"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) 5-Hydroxy-7-methoxy-4'-hydroxyflavone -6-O-β-D-glycoside 0.0001%
6) Purified water remainder

"Formulation 3"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) 5-Methoxy-6,7-methylenedioxy isoflavone -4'-O-β-D-glycoside 0.001%
6) Purified water remainder

"Formulation 4"

1) Glycerol 4.0%
2) 1,3-butylene glycol 4.0%
3) Ethanol 7.0%
4) Polyoxyethylene oleyl alcohol (20 mol) 0.5%
5) isoflavone-7-β-D-glycoside 0.0002%
6) Purified water remainder

-- Evaluative criteria for roughness of skin --

Markedly effective:	Rough skin was essentially not pronounced after 1 week.
Effective:	Rough skin was extremely slight after 1 week.
Moderately effective:	Rough skin was fairly slight after 1 week.
Ineffective:	There was no change in rough skin after 1 week.

– Evaluations of rough skin –

◎: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was greater than 60%

O: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was 20% to 60%

X: Cases in which the percentage of subjects evaluated as markedly effective or effective (efficacy rate) was less than 20%

Table 3. Effectiveness in Improvement of Skin Roughness

Comparison Case 1	Formulation Case 1	Formulation Case 2	Formulation Case 3	Formulation Case 4
X	O	◎	◎	◎

The same formulation was used in Comparison Case 1 in Table 3 as in Compartison Case 1 except that hot water extract of Iris florentina L. extract was excluded.

As should be evident from Table 3, it was found that formulations in which flavone glycosides and isoflavone glycosides such as 5-hydroxy-7-methoxy-4'-hydroxyflavone-6-O-β-D-glycoside, 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glycoside, isoflavone-7-β-D-glycoside and Iris florentina L. hot water extract were compounded and had excellent effectiveness in improving skin roughness.

[Examples]

Next, we shall present a detailed description of this invention by means of examples. This invention is not limited by them. The quantities compounded are indicated as weight %. The compounding quantities of flavone glycoside and isoflavone glycoside are as dry substance.

Example 1, Toilet Water

(1) 5,4'-hydroxy-7-methoxyflavone-8-C-β-D-glycoside	1.0%
(2) Glycerol	4.0%
(3) 1,3-butylene glycol	4.0%
(4) Ethanol	7.0%
(5) Polyoxyethylene oleyl alcohol	0.5%
(6) Methylparaben	0.05%
(7) Citric acid	0.01%
(8) Sodium citrate	0.1%
(9) Fragrances	0.05%
(10) Purified water	remainder

(Preparation Method)

Citric acid, sodium citrate, glycerol and 1,3-butylene glycol were dissoved in purified water. Separately, polyoxyethylene oleyl alcohol, 5,4'-hydroxy-7-methoxyflavone-8-C-β-D-glycoside, fragrances and methylparaben were dissolved in ethanol. This solution was then added to the aforementioned purified water solution, solubilized and filtered, with toilet water being obtained.

Example 2, Cream

(1) Cetostearyl alcohol	3.5%
(2) Squaiane	40.0%
(3) Beeswax	3.0%
(4) Reduced lanolin	5.0%
(5) Ethylparaben	0.3%
(6) Polyoxyethylene (20) sorbitan monopalmitic acid ester	2.0%
(7) Stearic acid monoglyceride	2.0%
(8) 5-hydroxy-7-methoxy-4'-hydroxyflavone -6-C-β-D-glucoside	0.000001%
(9) Fragrances	0.03%
(10) 1,3-butylene glycol	5.0%
(11) Glycerol	5.0%
(12) Sodium hyaluronate	0.05%
(13) Purified water	remainder

(Preparation Method)

A solution that was obtained by heating and dissolving (1), (2), (3), (4), (5), (6), (7), (8) and (9) and maintaining it at 75°C was added to (10), (11), (12) and (13) that had been heated to 75°C as the materials were being stirred. The mixture was treated in an homogenizer and the emulsified particles were finely pulverized, after which it was rapidly cooled, with a cream being obtained.

Example 3, Emulsion

(1) 5-methoxy-6,7-methylenedioxy isoflavone -4'-O-β-D-glucoside	0.001%
(2) Stearic acid	1.5%
(3) Cetyl alcohol	0.5%
(4) Beeswax	2.0%
(5) Polyoxyethylene (10) monooleic acid ester	1.0%
(6) Glycerol monostearic acid ester	1.0%
(7) Quince seed extract (5% aqueous solution)	20.0%

(8) Propylene glycol	5.0%
(9) Ethanol	3.0%
(10) Ethylparaben	0.3%
(11) Fragrances	0.03%
(12) Purified water	remainder

(Preparation Method)

The 5-methoxy-6,7-methylenedioxy isoflavone-4'-O-β-D-glucoside and fragrances were added to ethanol and dissolved (alcohol phase). Propylene glycol was added to purified water in which it was dissolved by heating and maintained at 70°C (aqueous phase). The other components except for the quince seed extract were mixed in, dissolved by heating and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and preliminary emulsification was performed, with uniform emulsification being effected with an homogenizer. The alcohol phase and the quince seed extract were added as the mixture was being stirred. Following that, the materials were cooled to 30°C, with an emulsion being obtained.

Example 4, Pack

(1) Isoflavone-7-O-β-D-glucoside	0.1%
(2) Polyvinyl alcohol	15.0%
(3) Polyethylene glycol	3.0%
(4) Propylene glycol	7.0%
(5) Ethanol	10.0%
(6) Methylparaben	0.05%
(7) Fragrances	0.05%
(8) Purified water	remainder

(Preparation Method)

Polyethylene glycol, propylene glycol and methylparaben were added to purified water and were dissolved by stirring. Next, the polyvinyl alcohol was added and was heated and stirred. An ethanol solution in which the isoflavone-7-O-β-D-glucoside and fragrances were dissolved was added and the mixture was dissolved by heating, with a pack being obtained.

Example 5, Cosmetic Material for Scalp Use

(1) 5-hydroxy-6,4'-methoxyisoflavone-7 -O-β-D-glucoside	2.0%
(2) 1,3-butylene glycol	6.5%
(3) Polyethylene glycol 1500	5.0%
(4) Ethanol	5.5%
(5) Potassium hydroxide	0.05%
(6) Purified water	45.45%
(7) 2-hexyldecylpalmitate	10.0%
(8) Squalane	5.0%
(9) Butylparaben	0.2%
(10) Vitamin C	0.15%
(11) Fragrances	0.05%
(12) Purified water	19.9%
(13) Carboxyvinyl polymer	0.2%

(Preparation Method)

A solution comprised of (7), (8), (9), (10) and (11) that had been dissolved at 75°C was added to (1), (2), (3), (4) and (6), which were being maintained at 75°C as the materials were being stirred. Further, (5), (12) and (13) were added at room temperature as they were being dissolved by stirring. The solution was then cooled while being stirred, with a scalp treatment being obtained.

Example 6, Ointment

(1) 5-methoxy-6,7-methylenedioxyisoflavone -4-O-β-D-glucoside	5.0%
(2) Stearyl alcohol	18.0%
(3) Vegetable wax	20.0%
(4) Polyoxyethylene (10) monooleic acid ester	0.25%
(5) Glycerol monostearic acid ester	0.25%
(6) Vaseline	40.0%
(7) Purified water	16.5%

(Preparation Method)

The purified water was maintained at 70°C (aqueous phase). The other constituents were mixed and dissolved at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and emulsification to a homogeneous state was effected with an homogenizer, after which the emulsion was cooled and an ointment was obtained.

Example 7, Toilet Water

(1) 5,4'-hydroxyflavone-8-O-β-D -glucoside	0.00003%
(2) 5-methoxy-6,7-methylenedioxyisoflavone- -4'-O-β-D-glucoside	0.00002%
(3) Glycerol	4.0%
(4) 1,3-butylene glycol	4.0%
(5) Ethanol	7.0%
(6) Polyoxyethylene oleyl alcohol	0.5%
(7) Methylparaben	0.05%
(8) Citric acid	0.01%

(9) Sodium citrate	0.1%
(10) Fragrances	0.05%
(11) Purified water	remainder

(Preparation Method)

The citric acid, sodium citrate, glycerol and 1,3-butylene glycol were dissolved in the purified water. Separately, the 5,4'-hydroxyflavone-8-O-β-D-glucoside, 5-methoxy-6,7-methylenedioxyisoflavone-4'-O-β-D-glucoside, fragrances and methylparaben were dissolved in ethanol, this solution was added to the aforementioned purified water solution and the mixture was solubilized and filtered, with toilet water being obtained.

The cosmetic materials obtained in Examples 1 to 7 exhibited superior effectiveness in wound healing, preventing and improving skin roughness and in preventing aging in terms of sagging of the skin and loss of luster.

Applicant: Shiseido Company, Ltd.